Amendments to the Specification:

Please replace the paragraphs beginning at page 24, line 15, thru page 25, line 27, with the following amended paragraph:

Figure 1a depicts the results of LCMS analysis of recombinant ~~MM-416776~~ SEQ ID NO:26 peptide and ~~MD-915~~ SEQ ID NO:28 peptide.

Figures 1b and c depict the results of LCMS analysis of synthetic ~~MD-1100~~ SEQ ID NO:31 peptide and the blank.

Figure 2 depicts the results of the intestinal GC-C receptor activity assay of synthetic ~~MM-416776~~ SEQ ID NO:26 peptide, ~~MD-915~~ SEQ ID NO:28 peptide and two different ~~MD-1100~~ SEQ ID NO:31 peptides.

Figure 3a depicts the effect of recombinant ~~MM-416776~~ SEQ ID NO:26 peptide and Zelnorm® in a murine gastrointestinal transit model.

Figure 3b depicts the effect of synthetic ~~MD-1100~~ SEQ ID NO:31 peptide and Zelnorm® in an acute murine gastrointestinal transit model.

Figure 3b depicts the effect of synthetic ~~MD-1100~~ SEQ ID NO:31 peptide and Zelnorm® in an chronic murine gastrointestinal transit model.

Figures 4a and 4b depict the effect of peptides ~~MD-915, MD-1100, and MM-416776~~ SEQ ID NO:28, SEQ ID NO:31, and SEQ ID NO:26 in an acute murine gastrointestinal transit model.

Figure 4c depicts the effect of ~~MD-1100~~ SEQ ID NO:31 peptide in a chronic murine gastrointestinal transit model.

Figure 5a depicts the effect of ~~MM-416776~~ SEQ ID NO:26 peptide and Zelnorm® in a suckling mouse intestinal secretion model.

Figure 5b depicts the effects of ~~MD-1100~~ SEQ ID NO:31 and Zelnorm® in a mouse intestinal secretion model.

Figures 6a and 6b depict the effects of ~~MM-416776, MD-1100 and MD-915~~ SEQ ID NO:26, SEQ ID NO:31, and SEQ ID NO:28 peptides in a mouse intestinal secretion model.

Figure 7 shows the results of experiment in which ~~MD-1100~~ SEQ ID NO:31 activity was analyzed in the TNBS colonic distention model.

Figures 8a and 8b show the effects of differing doses of ~~MD-915 and MD-1100~~ SEQ ID NO:28 and SEQ ID NO:31 in the PBQ writhing assay.

Figure 9 shows the results of Kd determination analysis using ~~MD-1100~~ SEQ ID NO:31 in a competitive radioligand binding assay.

Figures 10a and 10b show bioavailability data for IV and orally administered ~~MD-1100~~ SEQ ID NO:31 as detected by an ELISA assay and LCMS.

Please replace the paragraph beginning at page 30, line 29, thru page 32, line 11, with the following amended paragraph:

Thus, useful variants based on the core sequence include:

Asn Ser Ser Asn Tyr Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr
(SEQ ID NO:26; ~~MM-416776~~)

Asn Ser Ser Asn Tyr Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Trp Gly Cys Tyr
(SEQ ID NO:27)

Asn Ser Ser Asn Tyr Cys Cys Glu Tyr Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr
(SEQ ID NO:28; ~~MD-915~~)

Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr (SEQ ID NO:29; ~~MM416774~~)

Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Trp Gly Cys Tyr (SEQ ID NO:30)

Cys Cys Glu Tyr Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr (SEQ ID NO:31; ~~MD-1100~~)

Asn Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr (SEQ ID NO:32)

Asn Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Trp Gly Cys Tyr (SEQ ID NO:33)

Asn Cys Cys Glu Phe Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr (SEQ ID NO:34)

Asn Cys Cys Glu Tyr Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr (SEQ ID NO:35)

Asn Cys Cys Glu Trp Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr (SEQ ID NO:36)

Asn Cys Cys Glu Arg Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr (SEQ ID NO:37)

Asn Cys Cys Glu Lys Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr (SEQ ID NO:38)

Asn Ser Ser Asn Tyr Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:39)

Asn Ser Ser Asn Tyr Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Trp Gly Cys Tyr Asp Phe (SEQ ID NO:40)

Asn Ser Ser Asn Tyr Cys Cys Glu Phe Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:41)

Asn Ser Ser Asn Tyr Cys Cys Glu Tyr Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:42)

Asn Ser Ser Asn Tyr Cys Cys Glu Trp Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:43)

Asn Ser Ser Asn Tyr Cys Cys Glu Arg Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:44)

Asn Ser Ser Asn Tyr Cys Cys Glu Lys Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:45)

Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:46)

Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Trp Gly Cys Tyr Asp Phe (SEQ ID NO:47)

Cys Cys Glu Phe Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:48)

Cys Cys Glu Tyr Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:49)

Cys Cys Glu Trp Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:50)

Cys Cys Glu Arg Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:51)

Cys Cys Glu Lys Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:52)

Asn Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:53)

Asn Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Trp Gly Cys Tyr Asp Phe (SEQ ID NO:54)

Asn Cys Cys Glu Phe Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:55)

Asn Cys Cys Glu Tyr Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:56)

Asn Cys Cys Glu Trp Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:57)
Asn Cys Cys Glu Arg Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:58)
Asn Cys Cys Glu Lys Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr Asp Phe (SEQ ID NO:59)

Please replace the paragraph beginning at page 36, line 26, with the following amended paragraph:

A variant ST peptide, referred to as ~~MD-915~~ SEQ ID NO:28, was reproduced recombinantly and tested in an animal model. ~~MD-915~~ SEQ ID NO:28 has the sequence: Asn Ser Ser Asn Tyr Cys Cys Glu Tyr Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr (SEQ ID NO:28). A peptide having the sequence of the wild-type ST peptide was also created (~~MM-416776~~ SEQ ID NO:26).

Please replace the paragraph beginning at page 37, line 1, with the following amended paragraph:

~~MD-915 and MM-416776~~ SEQ ID NO:28 and SEQ ID NO:26 peptides were produced as preproproteins using vectors produced as follows. A sequence encoding a heat-stable enterotoxin pre-pro sequence was amplified from pGK51/pGSK51 (ATCC 67728) using oligonucleotide MO3514 (5' CACACCATATGAAGAAATCAATATTATTTATTTTCTTTCTG 3' (SEG ID NO:60)) and oligonucelotide MO3515 (5' CACACCTCGAGTTAGGTCTCCATGCTTTCAGGACCACTTTTATTAC 3' (SEQ ID NO: 61)). The amplification product fragment was digested with NdeI/XhoI and ligated to the T7 expression vector, pET26b(+) (Novagen) digested with NdeI/XhoI thereby creating plasmid MB3976. The region encoding the pre-pro protein was sequenced and found to encode the amino acid sequence: mkksilfiflsvlsfspfaqdakpagsskekitleskkcnivkk**s**n**k**s**g**pesm (SEQ ID NO: 24) which differs from the amino acid sequence of heat-stable enterotoxin a2 precursor (sta2; mkksilfiflsvlsfspfaqdakpagsskekitleskkcnivkknnesspesm (SEQ ID NO:25); GenBank® Accession No. Q47185, GI: 3913876) at three positions (indicated by underlining and bold text)

near the C-terminus. To create expression vectors with the pre-pro sequence, complementary oligos encoding each ST peptide variant or wild-type ST peptide were annealed and cloned into the MB3976 expression vector. To create MB3984 (encoding ~~MM-416776~~ SEQ ID NO:26 peptide full length wild-type ST peptide as a prepro protein), containing the amino acid sequence, NSSNYCCELCCNPACTGCY (SEQ ID NO:26) fused downstream of the pre-pro sequence, MB 3976 was digested with BsaI/XhoI and ligated to annealed oligos MO3621 (5' GCATGAATAGTAGCAATTACTGCTGTGAATTGTGTTGTAATCCTGCTTGTACCGGGT GCTATTAATAAC 3' (SEQ ID NO:62)) and MO3622 (5' TCGAGTTATTAATAGCACCCGGTACAAGCAGGATTACAACACAATTCACAGCAGTA ATTGCTACTATTC 3'(SEQ ID NO:63)). To create MB3985 (encoding ~~MD-915~~ SEQ ID NO:28 as a prepro protein) containing the following amino acid sequence, NSSNYCCEYCCNPACTGCY (SEQ ID NO:28) fused downstream of the pre-pro sequence, MB 3976 was digested with BsaI/XhoI and ligated to annealed oligos MO3529 (5' GCATGAATAGTAGCAATTACTGCTGTGAATATTGTTGTAATCCTGCTTGTACCGGGT GCTATTAATAAC 3' (SEQ ID NO:64)) and MO3530 (5' TCGAGTTATTAATAGCACCCGGTACAAGCAGGATTACAACAATATTCACAGCAGTA ATTGCTACTATTC 3'(SEQ ID NO:65)).

Please replace the paragraph beginning at page 38, line 1, with the following amended paragraph:

The ~~MD-915~~ SEQ ID NO:28 peptide and the ~~MM-416776~~ SEQ ID NO:26 peptide were produced as follows. The expression vectors were transformed into *E. coli* bacterial host BL21 λ DE3 (Invitrogen). A single colony was innoculated and grown shaking overnight at 30°C in L broth + 25 mg/l kanamycin. The overnight culture was added to 3.2 L of batch medium (Glucose 25 g/l, Caseamino Acids 5 g/l, Yeast Extract 5 g/l, KH_2PO_4 13.3 g/l, $(NH_4)_2HPO_4$ 4 g/l, $MgSO_4$-$7H_20$ 1.2 g/l, Citric Acid 1.7 g/l, EDTA 8.4 mg/l, $CoCl_2$-$6H_2O$ 2.5 mg/l, $MnCl_2$-$4H_2O$ 15 mg/l, $CuCl_2$-$4H_20$ 1.5 mg/l, H_3BO_3 3 mg/l, Na_2MoO_4-$2H_20$ 2.5 mg/l, Zn Acetate-$2H_20$ 13 mg/l, Ferric Citrate 100 mg/l, Kanamycin 25 mg/l, Antifoam DF_20_4 1 ml/l) and fermented using the

following process parameters : pH 6.7 - control with base only (28% NH_4OH), 30°C, aeration : 5 liters per minute. After the initial consumption of batch glucose (based on monitoring dissolved oxygen (DO) levels), 1.5 L of feed medium (Glucose 700 g/l, Caseamino Acids 10 g/l, Yeast Extract 10 g/l, $MgSO_4$-$7H_20$ 4 g/l, EDTA 13 mg/l, $CoCl_2$-$6H_2O$ 4 mg/l, $MnCl_2$-$4H_2O$ 23.5 mg/l, $CuCl_2$-$4H_20$ 2.5 mg/l, H_3BO_3 5 mg/l, Na_2MoO_4-$2H_20$ 4 mg/l, Zn Acetate-$2H_20$ 16 mg/l, Ferric Citrate 40 mg/l, Antifoam DF_20_4 1 ml/l) was added at a feed rate controlled to maintain 20% DO. IPTG was added to 0.2 mM 2 hours post feed start. The total run time was approximately 40-45 hours (until feed exhaustion).

Please replace the paragraphs beginning at page 39, line 4, thru page 40, line 2, with the following amended paragraphs:

The ~~MD-915~~ SEQ ID NO:28 peptide and ~~MM-416776~~ SEQ ID NO:26 peptide fractions were analyzed by standard LCMS and HPLC. LCMS analysis revealed that ~~MD-915~~ SEQ ID NO:28 is more homogeneous than ~~MM-416776~~ SEQ ID NO:26 (see Figure 1a; note that ~~MD-915~~ SEQ ID NO:28 peptide exhibits fewer peaks (Panel B) than ~~MM-416776~~ SEQ ID NO:26 (Panel A)).

1b: Preparation of synthetic variant ST peptides and wild-type ST peptide

Peptides were chemically synthesized by a commercial peptide synthesis company. Varying yields of peptides were obtained depending on the efficiency of chemical synthesis. Thus, the four peptides, in decreasing order of yield were: Cys Cys Glu Tyr Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr (SEQ ID NO:31; ~~MD-1100~~), 10-20% yield; Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr (SEQ ID NO:29; ~~MM416774~~); Asn Ser Ser Asn Tyr Cys Cys Glu Tyr Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr (SEQ ID NO:28; ~~MD-915~~); Asn Ser Ser Asn Tyr Cys Cys Glu Leu Cys Cys Asn Pro Ala Cys Thr Gly Cys Tyr (SEQ ID NO:26 ~~MM-416776~~), <5% yield. Thus the specific amino acid changes introduced into the peptides can create improved manufacturing properties.

Figure 1b shows the total ion chromatograph profile of synthetically manufactured MD-1100. Figure 1c shows the total ion chromatograph profile of the control blank sample. There is one major peak present in the ~~MD-1100~~ SEQ ID NO:31 sample that is not also present in the control sample. Quantitative analysis suggests the ~~MD-1100~~ SEQ ID NO:31 is >98% pure.

Example 2: Activation of the intestinal GC-C receptor by a variant ST peptide and ST peptide

The ability of ~~MD-915, MM-416776, and MD-1100~~ SEQ ID NO:28, SEQ ID NO:26, and SEQ ID NO:31 to activate the intestinal GC-C receptor was assessed in an assay employing the T84 human colon carcinoma cell line (American Type Culture Collection (Bethesda, Md.). For the assays cells were grown to confluency in 24-well culture plates with a 1:1 mixture of Ham's F12 medium and Dulbecco's modified Eagle's medium (DMEM), supplemented with 5% fetal calf serum and were used at between passages 54 and 60.

Please replace the paragraphs beginning at page 40, line 15, thru page 40, line 21, with the following amended paragraphs:

Figure 2 shows the activity of chemically synthesized peptide variants in this GC-C receptor activity assay. In this assay, ~~MM-416776~~ SEQ ID NO:26 and two different ~~MD-1100~~ SEQ ID NO:31 peptides (~~MD-1100~~ SEQ ID NO:31(a) and ~~MD-1100~~ SEQ ID NO:31(b), synthesized by two different methods) had activity comparable to ~~MM-416776~~ SEQ ID NO:26. ~~MD-915 and MM-416776~~ SEQ ID NO:28 and SEQ ID NO:26 peptide were chemically synthesized in a manner identical to that of ~~MD-1100~~ SEQ ID NO:31(b).

Example 3: ~~MD-915 and MM-416776~~ SEQ ID NO:28 and SEQ ID NO:26 increase intestinal transit in mice

Please replace the paragraphs beginning at page 41, line 13, thru page 42, line 21, with the following amended paragraphs:

As can be seen in Figure 3a, b, wild-type ST peptide (~~MM-416776~~ SEQ ID NO:26, (Sigma-Aldrich, St Louis, MO; 0.1 mg/kg), synthetically manufactured ~~MD-1100~~ SEQ ID NO:31 and Zelnorm® (0.1 mg/kg), a drug approved for IBS that is an agonist for the serotonin

receptor 5HT4, increase gastrointestinal transit rate in this model. Figure 4a shows the result of a study demonstrating that intestinal transit rate increases with an increasing dosage of either recombinantly synthesized ~~MM-416776 or MD-915~~ SEQ ID NO:26 and SEQ ID NO:28. Figure 4b shows the results of a study demonstrating both chemically synthesized MM-416776 or MD-1100 peptide increase intestinal transit rates more than either Tris buffer alone or an equivalent dose of Zelnorm®.

The identical experiment was performed to determine if ~~MD-1100~~ SEQ ID NO:31 is effective in a chronic dosing treatment regimen. Briefly, 8 week old CD1 female mice are dosed orally once a day for 5 days with either ~~MD-1100~~ SEQ ID NO:31 (0.06mg/kg or 0.25mg/kg in 20mM Tris pH 7.5) or vehicle alone (20mM Tris pH 7.5). On the 5th day, a GIT assay is performed identical to that above except 200µl of a 10% charcoal solution is administered. Figure 4c shows the results of a study demonstrating both chemically synthesized ~~MD-1100~~ SEQ ID NO:31 or Zelnorm® are effective in a mouse gastrointestinal motility assay upon chronic dosing (daily for 5 days). The results are shown side by side with acute dosing (1 day).

Example 4: ~~MD-915~~ SEQ ID NO:28 peptide and ~~MM-416776~~ SEQ ID NO:26 peptide increase intestinal secretion in suckling mice (SuMi assay)

~~MM-416776~~ SEQ ID NO:26 peptide and ~~MD-915~~ SEQ ID NO:28 were tested for their ability to increase intestinal secretion using a suckling mouse model of intestinal secretion. In this model a test compound is administered to suckling mice that are between 7 and 9 days old. After the mice are sacrificed, the gastrointestinal tract from the stomach to the cecum is dissected ("guts"). The remains ("carcass") as well as the guts are weighed and the ratio of guts to carcass weight is calculated. If the ratio is above 0.09, one can conclude that the test compound increases intestinal secretion. Figure 5a shows a dose response curve for wild-type ST peptide (~~MM-416776~~ SEQ ID NO:26) in this model. Figure 5b shows dose response curve for the ~~MD-1100~~ SEQ ID NO:31 peptide in this model. These data show that wild-type ST peptide (purchased from TDT, Inc. West Chester, PA) and the MD-1100 peptide increase intestinal secretion. The effect of Zelnorm® was also studied. As can be seen from Figure 5, Zelnorm® at 0.2 mg/kg does not increase intestinal secretion in this model. Figure 6a shows a dose response

curve for the recombinant MM-416776 peptide described above and the recombinant ~~MD-915~~ SEQ ID NO:28 peptide described above. As can be seen from Figure 6a, both peptides increase intestinal secretion in this model. Similarly figure 6b shows a dose response curve for chemically synthesized ~~MD-915, MD-1100 and MM-416776~~ SEQ ID NO:28, SEQ ID NO:31 and SEQ ID NO:26 as well as wild-type ST peptide (purchased from Sigma-Aldrich, St Louis, MO).

Please replace the paragraph beginning at page 44, line 3, with the following amended paragraph:

Figure 7 shows the results of experiment in which ~~MD-1100~~ SEQ ID NO:31 activity was analyzed in the TNBS colorectal model. Significant decreases in abdominal response are observed at 0.3 μg/kg and 3 μg/kg ~~MD-1100~~ SEQ ID NO:31. These results demonstrate that ~~MD-1100~~ SEQ ID NO:31 reduces pain associated with colorectal distension in this animal model.

Please replace the paragraphs beginning at page 45, line 5, thru page 47, line 14, with the following amended paragraphs:

Figures 8a and 8b show the effect of different doses of ~~MD-915 and MD-1100~~ SEQ ID NO:28 and SE ID NO:31 in the PBQ writhing assay. Indomethacin, an NSAID (nonsteroidal anti-inflammatory drug) with known pain control activity, was used as the positive control in the assay. Significant reductions in writhings were observed for ~~MD-915~~ SEQ ID NO: 28 (1 mg/kg dose) and ~~MD-1100~~ SEQ ID NO:31 (2.5 mg/kg dose) compared to the vehicle control. Loss of efficacy at the highest dose tested has also been observed for multiple other compounds (such as 5HT-3 antagonists) tested in similar assays. The results of this study suggest that both ~~MD-915 and MD-1100~~ SEQ ID NO:28 and SEQ ID NO:31 have antinociceptive effects in this visceral pain model comparable to the intermediate doses of indomethacin.

Example 5: ~~MD-1100~~ SEQ ID NO:31 Kd determination

To determine the affinity of ~~MD-1100~~ SEQ ID NO:31 for GC-C receptors found in rat intestinal mucosa, a competition binding assay was performed using rate intestinal epithelial cells. Epithelial cells from the small intestine of rats were obtained as described by Kessler et al. (*J. Biol. Chem.* 245: 5281-5288 (1970)). Briefly, animals were sacrificed and their abdominal cavities exposed. The small intestine was rinsed with 300 ml ice cold saline or PBS. 10 cm of the small intestine measured at 10 cm from the pylorus was removed and cut into 1 inch segments. Intestinal mucosa was extruded from the intestine by gentle pressure between a piece of parafilm and a P-1000 pipette tip. Intestinal epithelial cells were placed in 2 ml PBS and pipetted up and down with a 5 ml pipette to make a suspension of cells. Protein concentration in the suspension was measured using the Bradford method (*Anal. Biochem.* 72: 248-254 (1976)).

A competition binding assay was performed based on the method of Giannella et al. (*Am. J. Physiol.* 245: G492-G498) between [^{125}I] labeled ~~MM-416776 and MD-1100~~ SEQ ID NO:26 and SEQ ID NO:31. The assay mixture contained: 0.5 ml of DME with 20 mM HEPES-KOH pH 7.0, 0.9 mg of the cell suspension listed above, 21.4 fmol[^{125}I]-~~MM-416776~~ SEQ ID NO:26 (42.8 pM), and different concentrations of competitor ~~MD-1100~~ SEQ ID NO:31 (0.01 to 1000 nM). The mixture was incubated at room temperature for 1 hour, and the reaction stopped by applying the mixture to GF/B glass-fiber filters (Whatman). The filters were washed with 5 ml ice-cold PBS and radioactivity was measured. Figure 9 shows that the Kd for ~~MD-1100~~ SEQ ID NO:31 in this assay is 4.5 nm. %B/Bo is the percentage of the ratio of radioactivity trapped in each sample (B) compared to the radioactivity retained in a control sample with no cold competitor (Bo). Giannella et al. (*Am. J. Physiol.*245: G492-G498) observed that the Kd for wild-type ST peptide in this same assay was ~13 nm.

Example 6: Pharmacokinetic properties of ~~MD-1100~~ SEQ ID NO:31

To study the pharmacokinetics of ~~MD-1100~~ SEQ ID NO:31, absorbability studies in mice were performed by administering ~~MD-1100~~ SEQ ID NO:31 intravaneously via tail vein injection or orally by gavage to 8-week-old CD1 mice. Serum was collected from the animals at various time points and tested for the presence of ~~MD-1100~~ SEQ ID NO:31 using a competitive

enzyme-linked immunoabsorbent assay (Oxoid, ST EIA kit, Cat#TD0700). The assay utilized monoclonal antibodies against ST peptide (antibodies are provided in the Oxoid kit) and synthetically manufactured ~~MD-1100~~ SEQ ID NO:31. Figure 10a show absorption data for intravenously and orally administered ~~MD-1100~~ SEQ ID NO:31 as detected by the ELISA assay. MD-1100 appears to be minimally systemically absorbed and is < 2.2% bioavailable.

A similar bioavailability study was performed in which LCMS rather than ELISA was used to detect ~~MD-1100~~ SEQ ID NO:31. Initially, serum samples were extracted from the whole blood of exposed and control mice, then injected directly (10mL) onto an in-line solid phase extraction (SPE) column (Waters Oasis HLB 25mm column, 2.0 x 15mm direct connect) without further processing. The sample on the SPE column was washed with a 5% methanol, 95% dH_2O solution (2.1 mL/min, 1.0 minute), then loaded onto an analytical column using a valve switch that places the SPE column in an inverted flow path onto the analytical column (Waters Xterra MS C8 5mm IS column, 2.1 x 20mm). The sample was eluted from the analytical column with a reverse phase gradient (Mobile Phase A: 10 mM ammonium hydroxide in dH_2O, Mobile Phase B: 10 mM ammonium hydroxide in 80% acetonitrile and 20% methanol; 20% B for the first 3 minutes then ramping to 95% B over 4 min. and holding for 2 min., all at a flow rate of 0.4 mL/min.). At 9.1 minutes, the gradient returns to the initial conditions of 20%B for 1 min. ~~MD-1100~~ SEQ ID NO:31 eluted from the analytical column at 1.45 minutes, and was detected by triple-quadrapole mass spectrometry (MRM, 764 (+2 charge state)>182 (+1 charge state) Da; cone voltage = 30V; collision = 20 eV; parent resolution = 2 Da at base peak; daughter resolution = 2 Da at base peak). Instrument response was converted into concentration units by comparison with a standard curve using known amounts of chemically synthesized ~~MD-1100~~ SEQ ID NO:31 prepared and injected in mouse serum using the same procedure.

Figure 10b shows absorption data for IV and orally administered ~~MD-1100~~ SEQ ID NO:31 as detected by LCMS. In this assay, ~~MD-1100~~ SEQ ID NO:31 appears similarly minimally systemically absorbed and is < 0.11 % bioavailable.